UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/520,248	03/07/2000	Sergio Abgrignani	CHIR-0234	9892

27476 7590 12/21/2004

Chiron Corporation
Intellectual Property - R440
P.O. Box 8097
Emeryville, CA 94662-8097

EXAMINER	
SCHWADRON, RONALD B	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/520,248	ABGRIGNANI, SERGIO	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 September 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): see enclosed action.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see enclosed action.*

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1,3,4,10 and 11.*

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☒ Other: *see enclosed action*

1. Claims 1,3,4,10,11 are under consideration.

2. The rejection of claims 5 and 6 under *35 U.S.C. § 112*, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention for the reasons elaborated in the previous Office Action is withdrawn in view of the cancellation of said claims.

3. The rejection of claims 5 and 6 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons elaborated in the previous Office Action is withdrawn in view of the cancellation of said claims.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1,3,4,10,11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Zimmerman et al. (U.S. Patent 5,425,940) in view of Clark et al. for the reasons elaborated in the previous Office action. Applicants arguments have been considered and deemed not persuasive.

Zimmerman et al. disclose in vivo administration of a combination of IL-2 and TNF-alpha (AKA TNF, wherein lymphotoxin is known in the art as TNF-beta) for treatment of tumors (see abstract). The combination of IL-2 and TNF-alpha are administered independent of antigen (they are administered without administration of antigen). The method results in antigen independent activation of T cells because the method has the same steps as the originally claimed method. The cells recited in claims 3 and 4 are present in vivo in humans (as are all possible types of immune cells which would be present in any individual in the absence of a specific genetic defect that would result in the absence of a particular cell population). Zimmerman et al. does not disclose the use of IL-6 with IL-2 and TNF. Clark et al. disclose that IL-6 can be used in cancer therapy (see abstract and column 6, second complete paragraph). Clark et al. disclose that IL-6 can be used in combination with other therapeutic agents (see column 5, third

paragraph). Clark et al. disclose that IL-6 can be used in combination with IL-2 for cancer therapy (see column 6, fifth paragraph). The combination of IL-2 and IL-6 are administered independent of antigen (they are administered without administration of antigen). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Zimmerman et al. disclose administration of a combination of IL-2 and TNF-alpha for treatment of tumors whilst Clark et al. disclose that IL-6 can be used in combination with IL-2 for cancer therapy. One of ordinary skill in the art would have been motivated to do the aforementioned because Clark et al. disclose that IL-6 can be used in combination with other therapeutic agents and that IL-6 can be used in combination with IL-2 for cancer therapy, whilst Zimmerman et al. disclose the advantages of using TNF and IL-2 for treating cancer (see abstract). The particular dosages recited in claims 5 and 6 would have determined by routine experimentation (while the dosages recited in the claim are indefinite for the reasons stated above, for the purpose of the prior art it will be assumed that they encompass a working embodiment of the claimed method).

Regarding applicants comments, the prior art method results in antigen independent activation of T cells because the method has the same steps as the originally claimed method. In addition, Zimmerman et al. disclose that their method activates T cells in vivo (see column 17, lines 7-12). Regarding applicants various unsupported speculations regarding expectation of success , the MPEP section 716.01(c) [R-2] states

II. >< ATTORNEY ARGUMENTS CANNOT TAKE THE PLACE OF EVIDENCE

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).

Regarding applicants comments about motivation to create the claimed invention, one of ordinary skill in the art would have been motivated to do the aforementioned because Clark et al. disclose that IL-6 can be used in combination with other therapeutic agents and that IL-6 can be used in combination with IL-2 for cancer therapy, whilst Zimmerman et al. disclose the advantages of using TNF and IL-2 for treating cancer (see abstract). Regarding applicants comments about synergistic effect as per the specification, page 12, said passage of the specification refers to an in vitro assay using

particular cells examined under particular conditions, wherein the claimed invention is drawn to an in vivo method of treatment. Therefore, the aforementioned teaching is not germane to the claimed invention. Regarding applicants comments, there is no evidence of record that the Clark et al. reference lacks enablement for the cited teachings. Regarding the purported unexpected results disclosed in the specification, they are not of the scope of the claimed invention (eg. the claimed invention is not drawn to an in vitro method).

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached Monday through Thursday from 7:30am to 6:00pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.
For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644